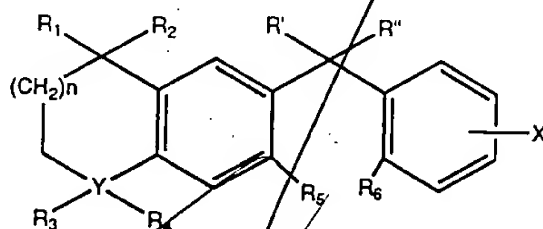


request amendment of the application as follows. Applicants also request consideration of the following Remarks.

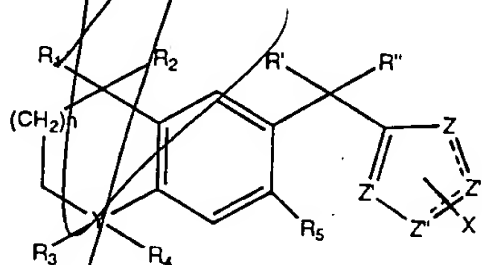
IN THE CLAIMS

Please amend claims 4, 15, 19, 27, 29, 30, 31, 32 as follows:

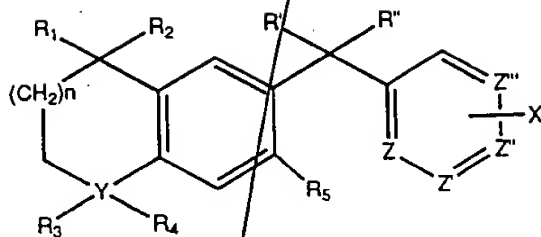
4. (Four Times Amended) A compound having the formula:



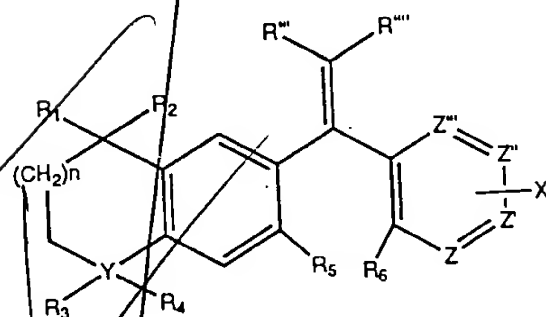
or



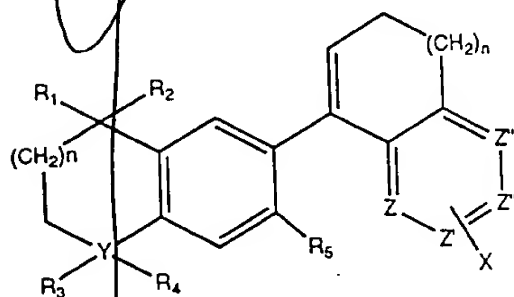
or



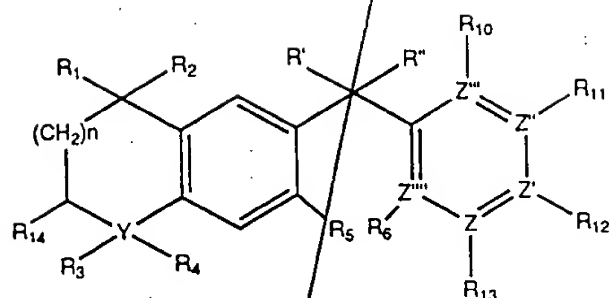
or



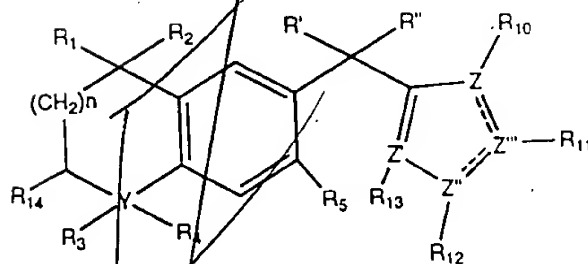
or



*Did  
cont'd*



or



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

$Y$  represents  $C$ ,  $O$ ,  $S$ ,  $N$ ,  $CHOH$ ,  $CO$ ,  $SO$ ,  $SO_2$ , or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where  $Y$  is  $C$  or  $N$ ;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if  $R'$  and  $R''$  represent H, OH,  $C_1-C_4$  alkoxy or  $C_1-C_4$  acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$  or  $(CF)_nCF_3$ , and exist only if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from which it originates is C, ~~for each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from~~

which it originates is N.] and where one of  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  or  $R_{13}$  is X;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_8$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_9$  represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where  $q=2-4$ ;

$R_{14}$  represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

$R_{17}$  represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes),  $R_9$ , alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, aryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole,  $PO_3H$ ,  $SO_3H$ , CHO,  $CH_2OH$ ,  $CONH_2$ , COSH,  $COOR_9$ ,  $COSR_9$ ,  $CONHR_9$ , or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO,  $CH_2OH$ ,  $COHN_2$ ,  $COOR_9$ , or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

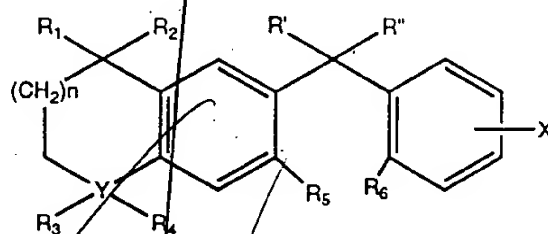
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a

single bond to another such Z which is N, and is not O or S in any  
of the six-membered rings containing them;

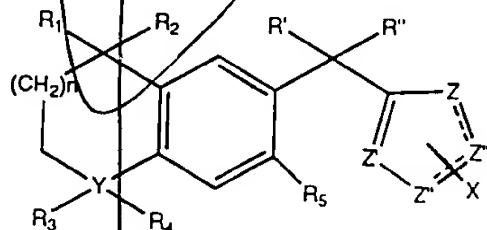
*Concluded*  
n = 0-3; and

the dashed lines in the second and seventh structures shown  
depict optional double bonds.

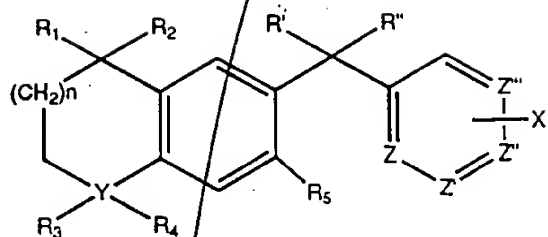
12.15. (Thrice Amended) A pharmaceutical composition  
comprising in a pharmaceutically acceptable vehicle suitable for  
enteral, parenteral, or topical administration, one or more  
compounds having the formula:



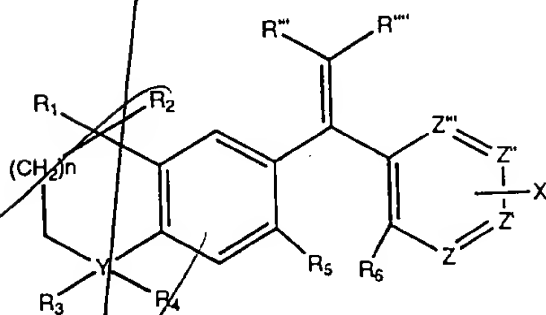
or



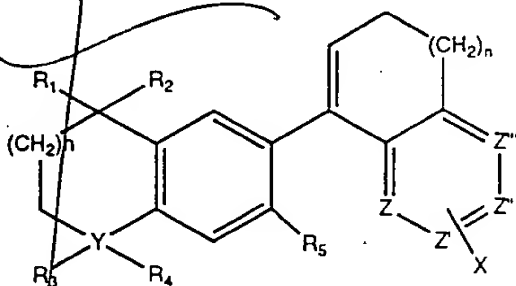
or



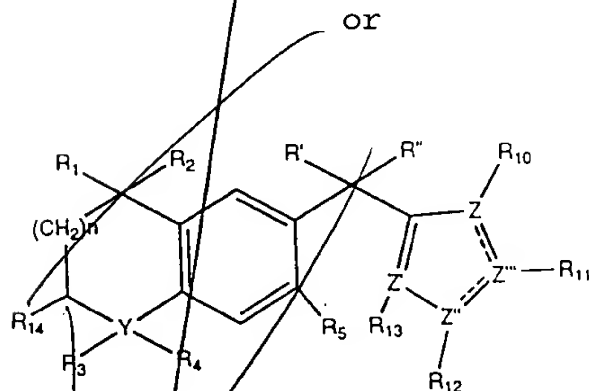
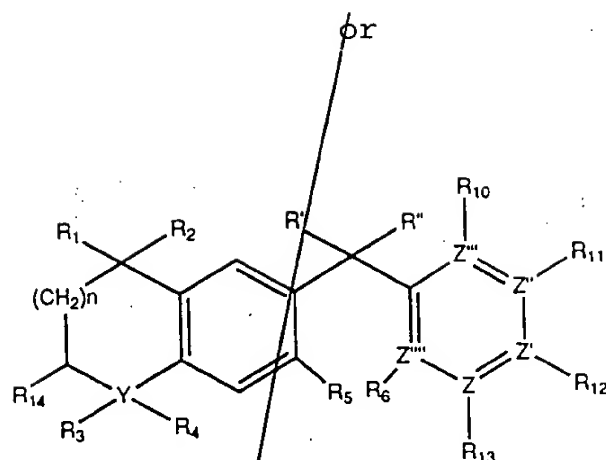
or



or



D<sup>2</sup>  
contd.



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

Y represents C, O, S, N, CHOH, CO, SO,  $SO_2$ , or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;



$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if  $R'$  and  $R''$  represent H, OH,  $C_1-C_4$  alkoxy or  $C_1-C_4$  acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$  or  $(CF)_nCF_3$ , and exist only if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from

which it originates is N,] and where one of  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  or  $R_{13}$  is X;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_8$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_9$  represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where  $q=2-4$ ;

$R_{14}$  represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

$R_{17}$  represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes),  $R_9$ , alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, aryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole,  $PO_3H$ ,  $SO_3H$ , CHO,  $CH_2OH$ ,  $CONH_2$ , COSH,  $COOR_9$ ,  $COSR_9$ ,  $CONHR_9$ , or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO,  $CH_2OH$ ,  $COHN_2$ ,  $COOR_9$ , or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

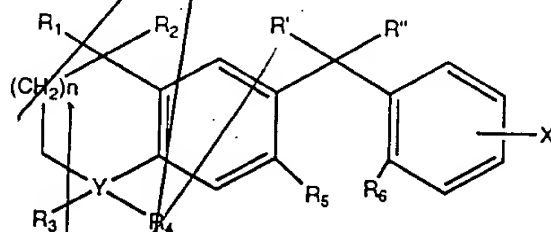
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a

single bond to another such Z which is N, and is not O or S in any  
of the six-membered rings containing them;

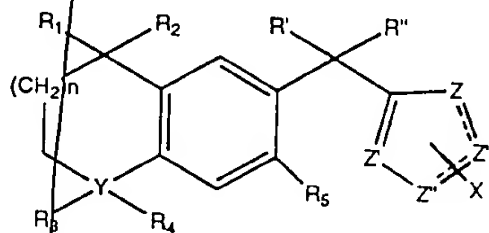
*D2 concluded*  
 $n = 0-3$ ; and

the dashed lines in the second and seventh structures shown  
depict optional double bonds.

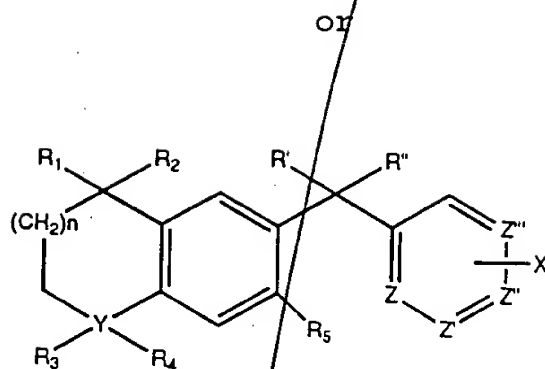
*16-18*. (Thrice Amended) A method for modulating a process  
mediated by one or more Retinoid X Receptors, said method  
comprising causing said process to be conducted in the presence of  
at least one compound having the formula:



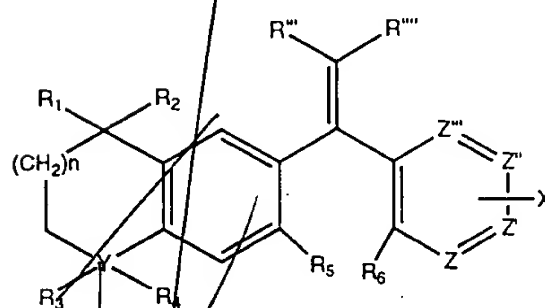
or



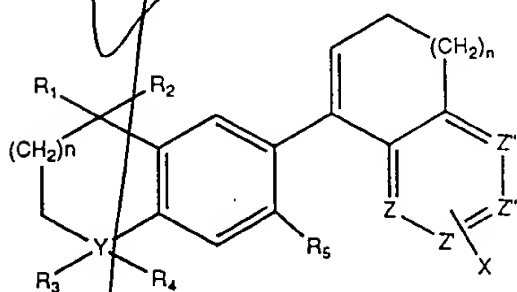
D<sup>3</sup>  
contid.



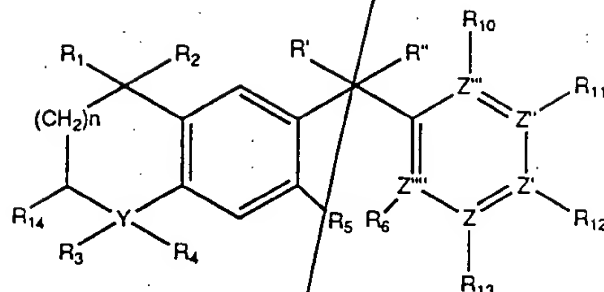
or



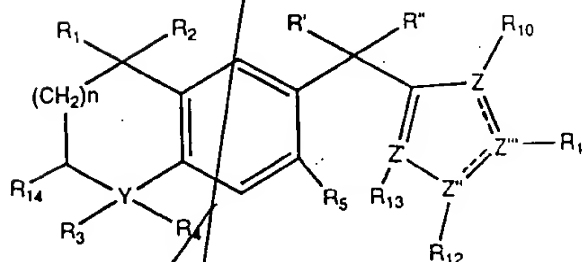
or



or



or



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

$Y$  represents C, O, S, N, CHOH, CO, SO, SO<sub>2</sub>, or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where  $Y$  is C or N;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if  $R'$  and  $R''$  represent H, OH,  $C_1-C_4$  alkoxy or  $C_1-C_4$  acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$  or  $(CF)_nCF_3$ , and exist only if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from

which it originates is N,1 and where one of  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  or  $R_{13}$  is X;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_8$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_9$  represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where  $q=2-4$ ;

$R_{14}$  represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

$R_{17}$  represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes),  $R_9$ , alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, aryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole,  $PO_3H$ ,  $SO_3H$ , CHO,  $CH_2OH$ ,  $CONH_2$ , COSH,  $COOR_9$ ,  $COSR_9$ ,  $CONHR_9$ , or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO,  $CH_2OH$ ,  $COHN_2$ ,  $COOR_9$ , or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

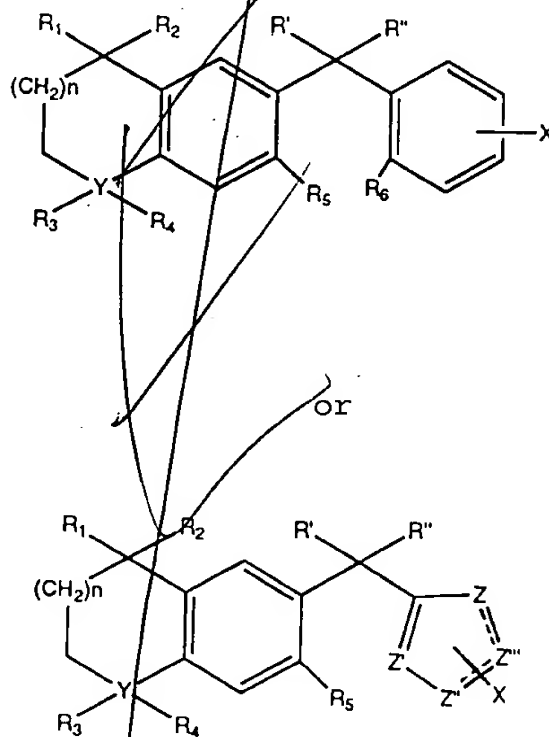
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a

single bond to another such Z which is N, and is not O or S in any  
of the six-membered rings containing them;

$n = 0-3$ ; and

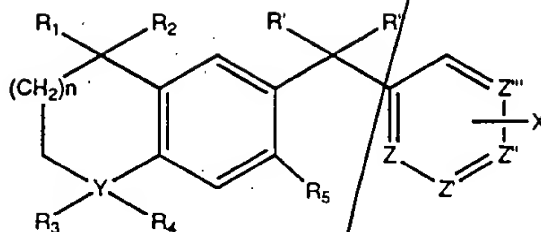
the dashed lines in the second and seventh structures shown  
depict optional double bonds.

24 27. (Thrice Amended) A method for modulating a process  
mediated by one or more Retinoid X Receptors, said method  
comprising administering to a mammalian subject an amount,  
effective to modulate said process mediated by said one or more  
Retinoid X Receptors, of one or more compounds having the formula:

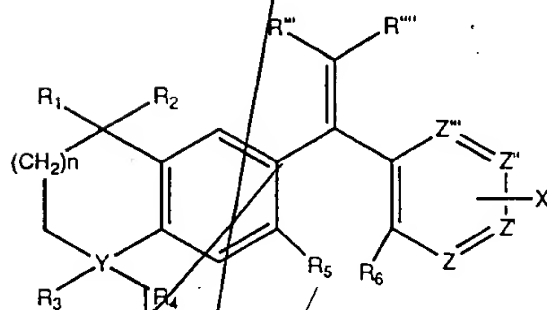




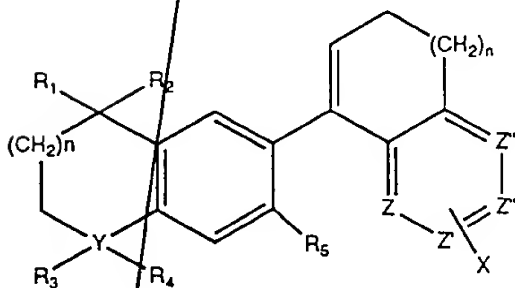
or



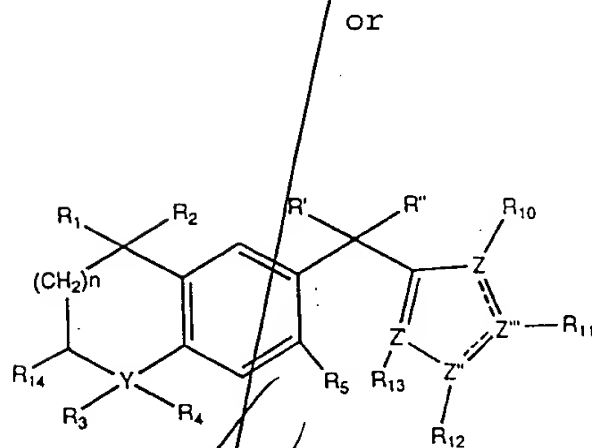
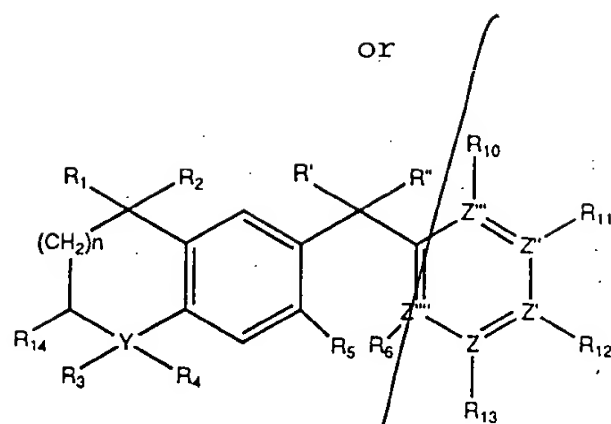
or



or



D4  
contd.



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

Y represents C, O, S, N, CHOH, CO, SO, SO<sub>2</sub>, or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy,

cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if  $R'$  and  $R''$  represent H, OH,  $C_1-C_4$  alkoxy or  $C_1-C_4$  acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$  or  $(CF)_nCF_3$ , and exist only if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from

which it originates is N,1 and where one of  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  or  $R_{13}$  is X;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_8$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_9$  represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where  $q=2-4$ ;

$R_{14}$  represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

*4*  
*contd.*  
 $R_{17}$  represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes),  $R_9$ , alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, aryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole,  $PO_3H$ ,  $SO_3H$ , CHO,  $CH_2OH$ ,  $CONH_2$ , COSH,  $COOR_9$ ,  $COSR_9$ ,  $CONHR_9$ , or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO,  $CH_2OH$ ,  $COHN_2$ ,  $COOR_9$ , or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

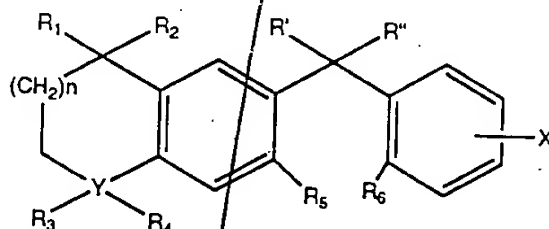
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a

single bond to another such Z which is N, and is not O or S in any  
of the six-membered rings containing them;

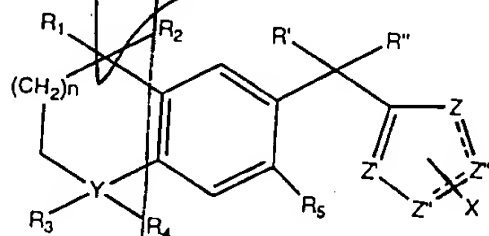
$n = 0-3$ ; and

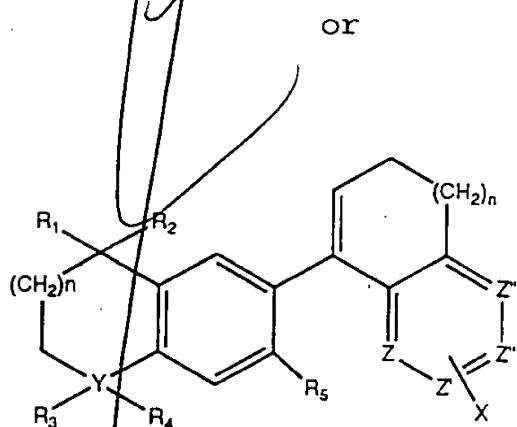
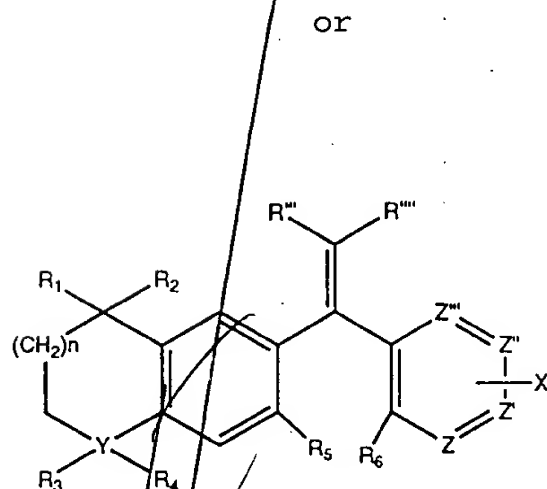
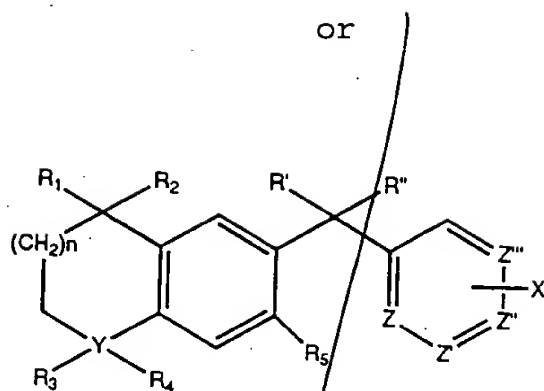
the dashed lines in the second and seventh structures shown  
depict optional double bonds.

26 25. (Thrice Amended) A method for treating a mammalian  
subject requiring Retinoid X Receptor therapy comprising  
administering to such subject a pharmaceutically effective amount  
of one or more compounds having the formula:



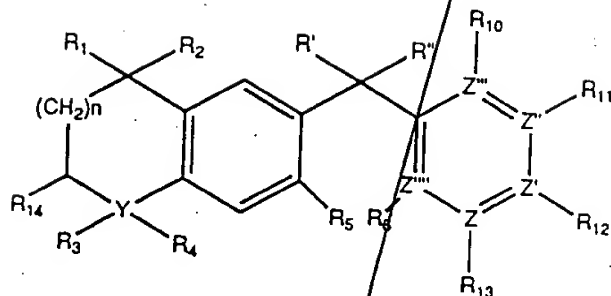
or



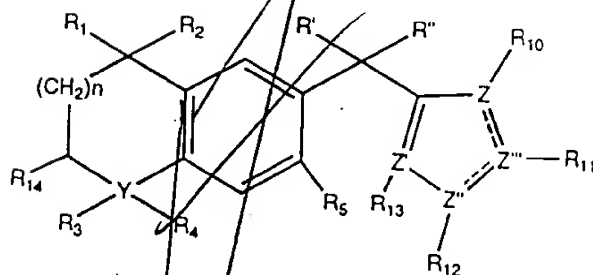


S5  
contd.

or



or



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

$Y$  represents  $C$ ,  $O$ ,  $S$ ,  $N$ ,  $CHOH$ ,  $CO$ ,  $SO$ ,  $SO_2$ , or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where  $Y$  is  $C$  or  $N$ ;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if  $R'$  and  $R''$  represent H, OH,  $C_1-C_4$  alkoxy or  $C_1-C_4$  acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$  or  $(CF)_nCF_3$ , and exist only if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from



which it originates is N,] and where one of  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  or  $R_{13}$  is X;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_8$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_9$  represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where  $q=2-4$ ;

$R_{14}$  represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

$R_{17}$  represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes),  $R_9$ , alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, aryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole,  $PO_3H$ ,  $SO_3H$ , CHO,  $CH_2OH$ ,  $CONH_2$ , COSH,  $COOR_9$ ,  $COSR_9$ ,  $CONHR_9$ , or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO,  $CH_2OH$ ,  $COHN_2$ ,  $COOR_9$ , or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

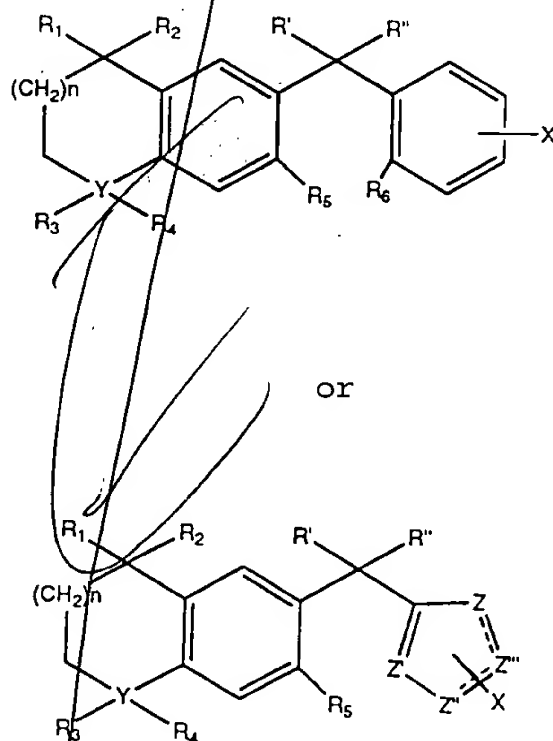
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a

single bond to another such Z which is N, and is not O or S in any  
of the six-membered rings containing them;

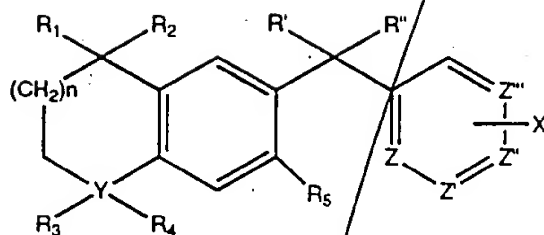
$n = 0-3$ ; and

the dashed lines in the second and seventh structures shown  
depict optional double bonds.

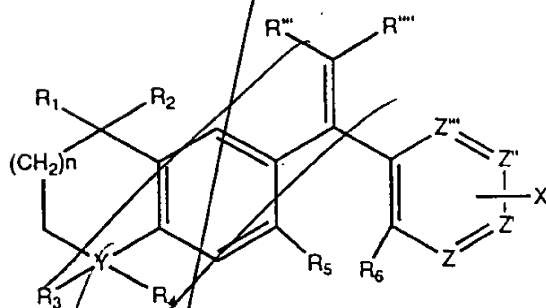
27<sup>30</sup>. (Thrice Amended) A method for increasing plasma  
concentrations of high density lipoprotein in a mammalian subject  
comprising administering to such subject a pharmaceutically  
effective amount of one or more compounds having the formula:



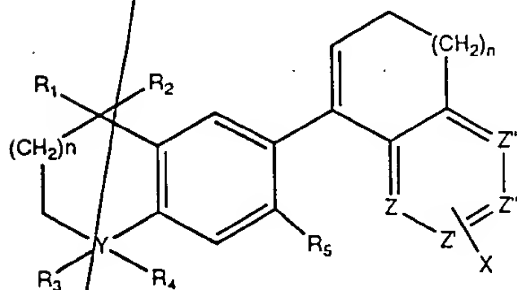
or



or

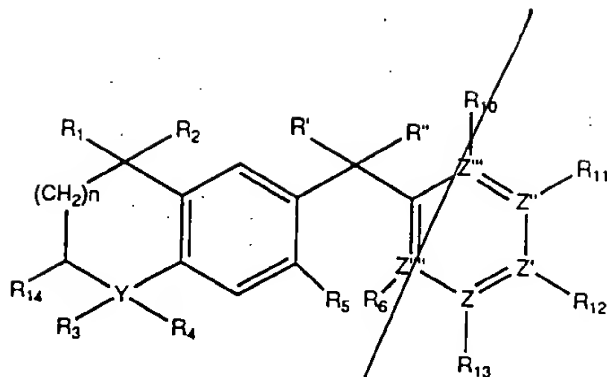


or

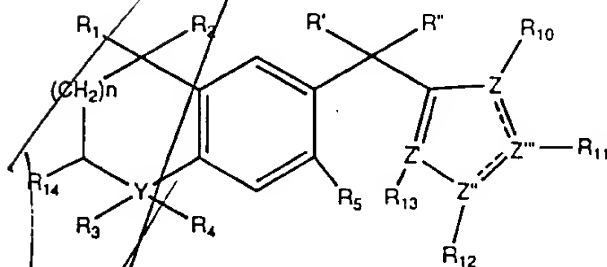


5  
cont'd.

or



or



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

Y represents C, O, S, N, CHOH, CO, SO, SO<sub>2</sub>, or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

*5*  
*cont'd*  
R<sub>4</sub> represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but R<sub>4</sub> does not exist if Y is N, and neither R<sub>3</sub> or R<sub>4</sub> exist if Y is S, O, CHOH, CO, SO, or SO<sub>2</sub>;

R' and R'' represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or R' or R'' taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R<sub>7</sub>R<sub>8</sub>)N-N=, R<sub>17</sub>O-N=, R<sub>17</sub>N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

R''' and R'''' represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or R''' and R'''' taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

R<sub>5</sub> represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub>, or (CF)<sub>n</sub>CF<sub>3</sub>, but R<sub>5</sub> cannot be hydrogen if R' and R'' represent H, OH, C<sub>1</sub>-C<sub>4</sub> alkoxy or C<sub>1</sub>-C<sub>4</sub> acyloxy or R' and R'' taken together form an oxo, methano, or hydroxyimino group;

R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub> each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR<sub>7</sub>, SR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub> or (CF)<sub>n</sub>CF<sub>3</sub>, and exist only if the Z, Z', Z'', Z''', or Z'''' from which it originates is C, or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z'''' from

which it originates is N,] and where one of  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  or  $R_{13}$  is X;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_8$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_9$  represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

$R_{14}$  represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

$R_{17}$  represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes),  $R_9$ , alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, aryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole,  $PO_3H$ ,  $SO_3H$ , CHO,  $CH_2OH$ ,  $CONH_2$ , COSH,  $COOR_9$ ,  $COSR_9$ ,  $CONHR_9$ , or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO,  $CH_2OH$ ,  $COHN_2$ ,  $COOR_9$ , or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

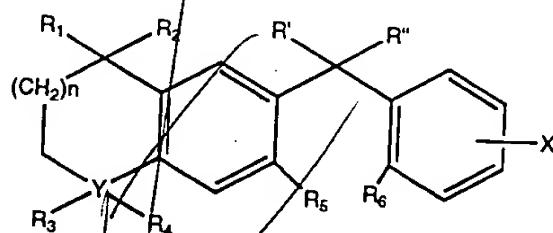
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a

single bond to another such Z which is N, and is not O or S in any  
of the six-membered rings containing them;

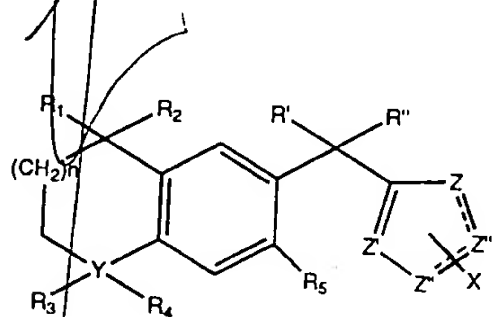
$n = 0-3$ ; and

the dashed lines in the second and seventh structures shown  
depict optional double bonds.

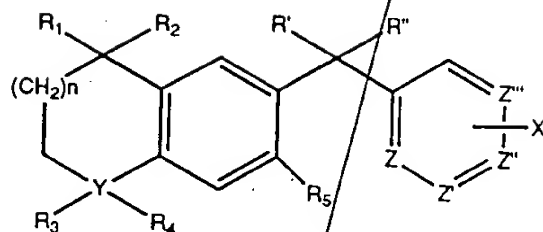
86 31. (Thrice Amended) A method for determining the  
presence of one or more Retinoid X Receptors comprising combining a  
compound as set forth below with a sample containing one or more  
unknown receptors and determining whether said compound binds to  
any receptor in said sample, said compound having the formula:



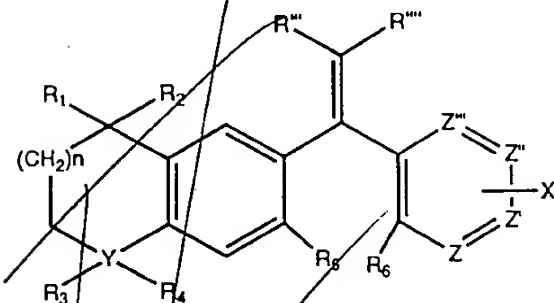
or



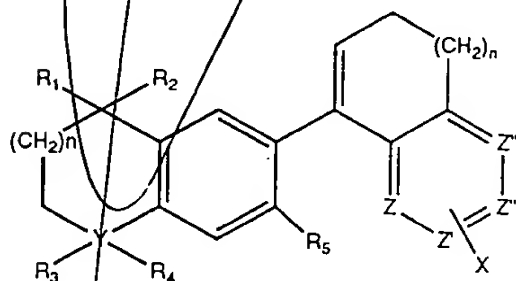
or



or



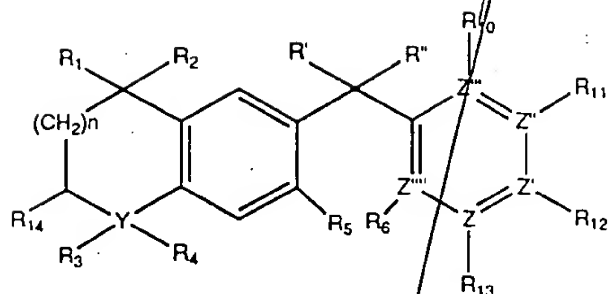
or



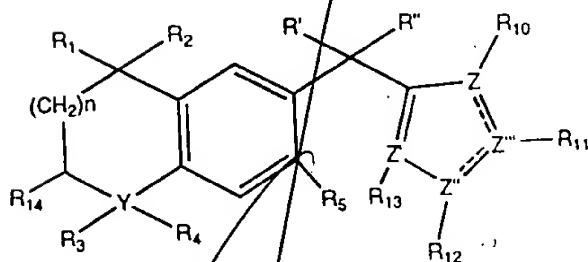
5  
cont'd.



or



or



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

Y represents C, O, S, N, CHOH, CO, SO,  $SO_2$ , or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if  $R'$  and  $R''$  represent H, OH,  $C_1-C_4$  alkoxy or  $C_1-C_4$  acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$  or  $(CF)_nCF_3$ , and exist only if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from

which it originates is N,] and where one of R<sub>6</sub>, R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub> or R<sub>13</sub> is X;

R<sub>7</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>8</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

R<sub>9</sub> represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R<sub>14</sub> represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

R<sub>17</sub> represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R<sub>9</sub>, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, aryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole, PO<sub>3</sub>H, SO<sub>3</sub>H, CHO, CH<sub>2</sub>OH, CONH<sub>2</sub>, COSH, COOR<sub>9</sub>, COSR<sub>9</sub>, CONHR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO, CH<sub>2</sub>OH, COHN<sub>2</sub>, COOR<sub>9</sub>, or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

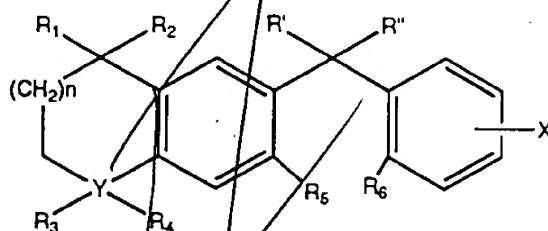
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a

single bond to another such Z which is N, and is not O or S in any of the six-membered rings containing them;

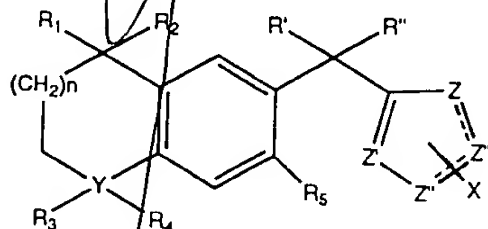
$n = 0-3$ ; and

the dashed lines in the second and seventh structures shown depict optional double bonds.

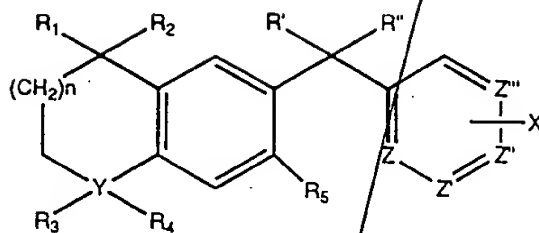
29 32. (Thrice Amended) A method of purifying Retinoid X Receptors comprising combining a compound as set forth below with a sample containing one or more said Retinoid X Receptors, allowing said compound to bind with Retinoid X Receptors, and separating out the bound combination of said compound and Retinoid X Receptor, said compound having the formula:



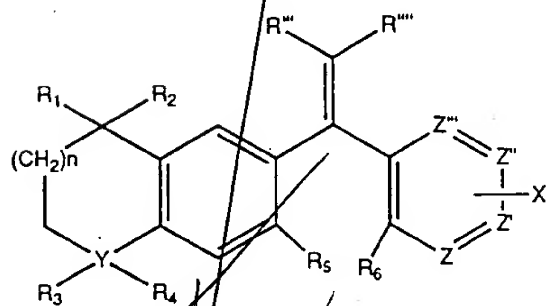
or



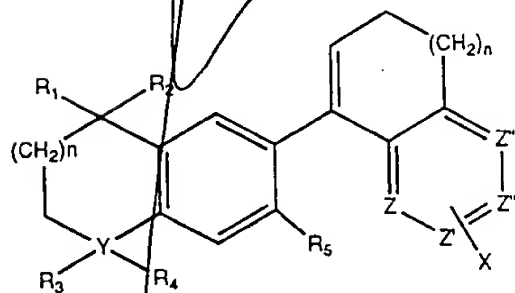
or

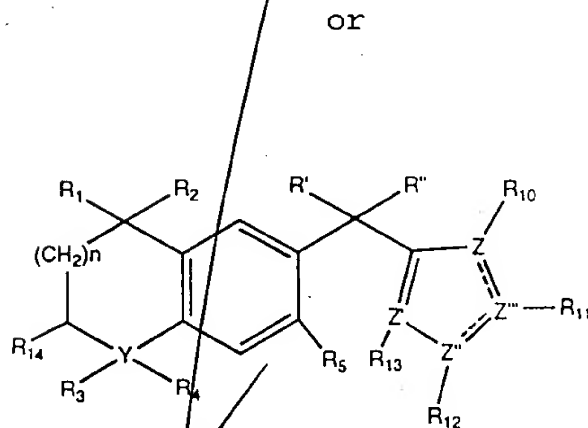
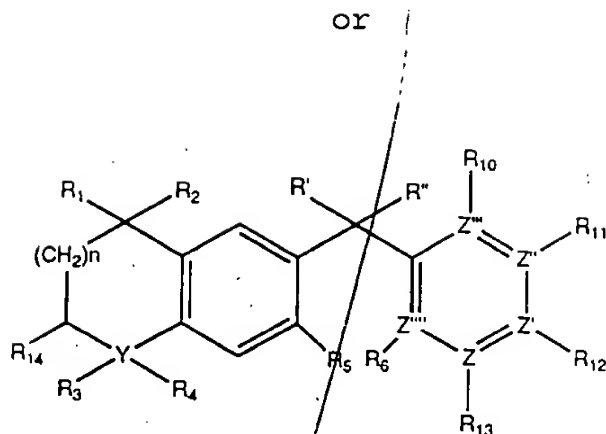


or



or





wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

$Y$  represents C, O, S, N, CHOH, CO, SO, SO<sub>2</sub>, or a pharmaceutically acceptable salt;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where  $Y$  is C or N;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S, O, CHOH, CO, SO, or  $SO_2$ ;

$R'$  and  $R''$  represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thio ether, or amino,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, thioketo,  $HO-N=$ ,  $NC-N=$ ,  $(R_7R_8)N-N=$ ,  $R_{17}O-N=$ ,  $R_{17}N=$ , epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

$R'''$  and  $R''''$  represent hydrogen, halogen, lower alkyl or acyl having 1-4 carbon atoms, alkyl amino,

or  $R'''$  and  $R''''$  taken together form a cycloalkyl group having 3-10 carbons, and wherein the cycloalkyl group can be substituted with lower alkyl having 1-4 carbons or halogen;

$R_5$  represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$ , or  $(CF)_nCF_3$ , but  $R_5$  cannot be hydrogen if  $R'$  and  $R''$  represent H, OH,  $C_1-C_4$  alkoxy or  $C_1-C_4$  acyloxy or  $R'$  and  $R''$  taken together form an oxo, methano, or hydroxyimino group;

$R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$ ,  $R_{13}$  each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro,  $OR_7$ ,  $SR_7$ ,  $NR_7R_8$  or  $(CF)_nCF_3$ , and exist only if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z,  $Z'$ ,  $Z''$ ,  $Z'''$ , or  $Z''''$  from

which it originates is N,] and where one of  $R_6$ ,  $R_{10}$ ,  $R_{11}$ ,  $R_{12}$  or  $R_{13}$  is X;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_8$  represents hydrogen or a lower alkyl having 1-6 carbons;

$R_9$  represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

$R_{14}$  represents hydrogen, a lower alkyl having 1-4 carbons, oxo, hydroxy, acyl having 1-4 carbons, halogen, thiol, or thioketone;

$R_{17}$  represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes),  $R_9$ , alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, aryl, OR, and SR, substituted alkenes);

X is COOH, tetrazole,  $PO_3H$ ,  $SO_3H$ , CHO,  $CH_2OH$ ,  $CONH_2$ , COSH,  $COOR_9$ ,  $COSR_9$ ,  $CONHR_9$ , or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring, provided, however, that X cannot be COOH, CHO,  $CH_2OH$ ,  $COHN_2$ ,  $COOR_9$ , or COOW where W is a pharmaceutically acceptable salt when X originates from a C in the 2 or 6 position on the ring;

Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a



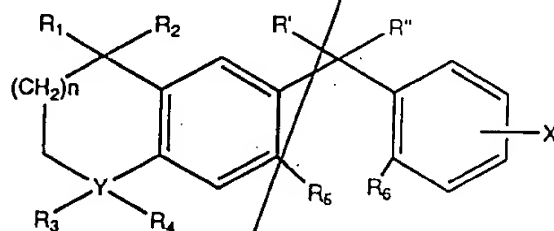
single bond to another such Z which is N, and is not O or S in any  
of the six-membered rings containing them;

$n = 0-3$ ; and

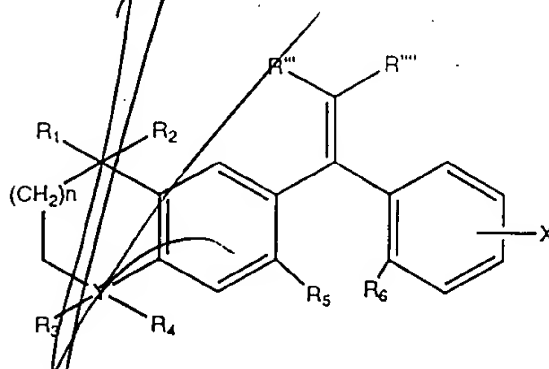
the dashed lines in the second and seventh structures shown  
depict optional double bonds.

In addition, please add the following new claims:

30. A compound having the formula:



or



wherein

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl having 1-4 carbon atoms;

Y represents C, O, S, or N;

$R_3$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

$R_4$  represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but  $R_4$  does not exist if Y is N, and neither  $R_3$  or  $R_4$  exist if Y is S or O;

$R'$  and  $R''$  represent hydrogen or lower alkyl having 1-4 carbon atoms,

or  $R'$  or  $R''$  taken together form an oxo (keto), methano, cyclopropyl or cycloalkyl group and wherein the cyclopropyl and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons;

$R'''$  and  $R''''$  represent hydrogen or lower alkyl having 1-4 carbon atoms,

$R_5$  represents hydrogen or a lower alkyl having 1-4 carbons or  $OR_7$ , but  $R_5$  cannot be hydrogen if  $R_6$  is hydrogen and  $R'$  and  $R''$  taken together form an oxo or a methano;

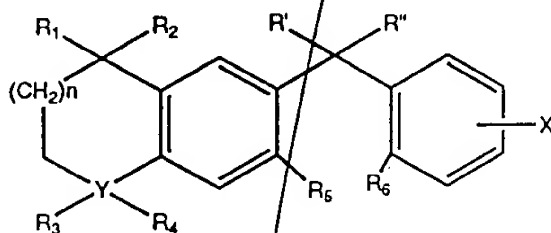
$R_6$  represents hydrogen;

$R_7$  represents hydrogen or a lower alkyl having 1-6 carbons;

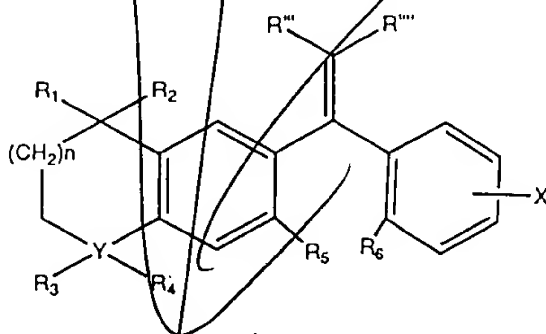
X is COOH and can originate from any C on the ring; and

$n = 0-1$ .

3) 63. A pharmaceutical composition for control of cellular processes regulated by retinoid compounds, Vitamin D, or thyroid hormone, comprising an effective regulating amount of a bicyclic aromatic compound, or a pharmaceutically acceptable ester, amide or salt thereof, in combination with a pharmaceutically acceptable carrier, wherein the bicyclic aromatic compound has the structural formula:



or



wherein:

$R_1$  and  $R_2$ , each independently, represent hydrogen or lower alkyl having 1-4 carbon atoms;

Y represents C, O, S, or N;

R<sub>3</sub> represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C or N;

R<sub>4</sub> represents hydrogen or lower alkyl having 1-4 carbon atoms where Y is C, but R<sub>4</sub> does not exist if Y is N, and neither R<sub>3</sub> or R<sub>4</sub> exist if Y is S or O;

R' and R'' represent hydrogen or lower alkyl having 1-4 carbon atoms,

*56 concluded*  
or R' or R'' taken together form an oxo (keto), methano, cyclopropyl or cycloalkyl group and wherein the cyclopropyl and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons;

R''' and R'''' represent hydrogen or lower alkyl having 1-4 carbon atoms,

R<sub>5</sub> represents hydrogen or a lower alkyl having 1-4 carbons or OR<sub>7</sub>, but R<sub>5</sub> cannot be hydrogen if R<sub>6</sub> is hydrogen and R' and R'' taken together form an oxo or a methano;

R<sub>6</sub> represents hydrogen;

R<sub>7</sub> represents hydrogen or a lower alkyl having 1-6 carbons;

X is COOH and can originate from any C on the ring; and

n = 0-1.